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Chromosomal localization of multiple genes encoding calmodulin

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Calmodulin (CaM) is an ubiquitous and highly conserved Ca^{2+}-binding protein involved in a number of important Ca^{2+}-modulated cellular processes including regulation of the cell cycle. Although only one form of calmodulin has been found in humans, 3 distinct human cDNA's have been isolated which encode the identical polypeptide. The corresponding loci have been designated CaMI, CaMII and CaMIII (1 - 5). The existence of three expressible genes for calmodulin may indicate that one is a housekeeping gene and that the additional copies are differentially regulated to modulate calmodulin function.

A panel of human/rodent somatic cell hybrids was used to determine the chromosomal localization of the 3 human calmodulin genes. The mapping panel used was largely made up of hybrid cell lines each of which contain a derivative chromosome 5 and which serendipitously also stably maintain 1, or in a few cases 2, additional human chromosomes. The parental CHO cell line used to construct most of the hybrids was UCW56 which harbors a LARS gene mutation which encodes a temperature-sensitive leucyl-tRNA synthetase. This temperature-sensitive phenotype is complimented by the human LARS gene product thus allowing for the selection at 39°C of hybrids retaining a human chromosome 5. Four additional hybrids were included which used other modes of selection specific for the retention of chromosome X, 12 or 18. Together, the 24 hybrids encompass the human genome and allow for the assignment of probes to any one of the 24 distinct human chromosomes.

The cDNA probe for CaMI (DD132, reference 1) was localized to chromosome 14 with cross-hybridization evident on chromosome 7 and very weakly on chromosome X. The assignments to chromosome 14 and 7 confirm an earlier report by Scrambler et al. (6).

The cDNA probe for CaMII (p27-1, reference 2) has not been definitively mapped at this time due to the existence of 3 known pseudogenes with 89.1, 93.8 and 95.3% homology with the coding sequence of CaMII (7,8).

Hybridization of p27-1 was observed for chromosomes 10, 13 17 and X. One of the known pseudogenes (hCE2) was isolated from a chromosome 17 library (7). Judging by the strength of the hybridization signal, the CaMII locus has been tentatively assigned to chromosome 10. The distribution of CaMII and its pseudogenes and CaMI and its probable pseudogenes is interesting since it shows no clustering with the exception of the CaMI and CaMII cross-hybridization to chromosome X. It is quite possible that both probes are detecting the same X chromosome locus.

The cDNA probe for CaMIII (p6-4, reference 3) was unequivocally assigned to chromosome 19. There was no apparent cross-hybridization to other chromosomes.

In conclusion, the calmodulin multigene family in humans has 3 expressed loci on 3 different chromosomes which encode the identical polypeptide. CaMI is located on chromosome 14, CaMII likely on chromosome 10 and CaMIII on chromosome 19. In addition, multiple pseudogenes are widely distributed in the genome. The stable maintenance within the genome of 3 genes encoding the same protein indicates that they all must play an important role in the overall regulation of calmodulin expression.

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